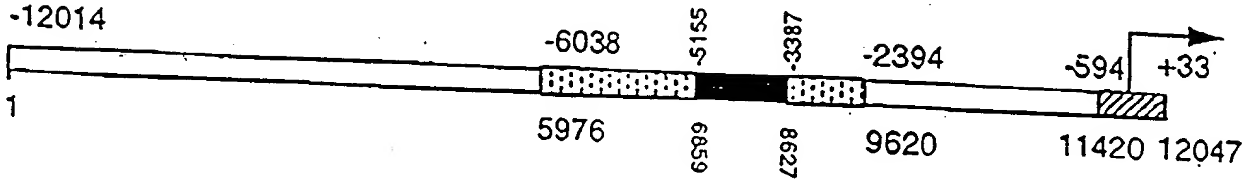

-12014
-6038
-5155
-3387
-2394
-594
+33
1
5976
6859
8627
9620
11420
12047

FIGURE 1

```
HKLK2.LA0   (6998)   AA-CTGAGCCTTGATTATATTG-GAGCTTGGTTGCA-CAG-ACATGTCGA
                     :: :: :: : ::: :::: :: : :::     :  ::: :::  :: :
PSE         ( 509)   AATCT-AG-C-TGA-TATAGTGTG-GCTCAAAACCTTCAGCACAAATC-A

HKLK2.LA0   (7044)   CCACCTTCATGGCTGAACTTTAGTACTTAGCCCCTCCAGACGTCTACAGC
                      :::: : : : ::  : : : ::   : :   : ::: ::  :: :::
PSE         ( 553)   -CACCGTTA-GACT--A-TCTGGT--GT-G--GC-CCAAAC--CTTCAGG

HKLK2.LA0   (7094)   TGATAGGCTGTAACCCAACAT-TGTCACCATAAATCACATTGTTAGACTA
                     ::: :    :  :: : : :: :: ::  :: : :: ::     :: : :
PSE         ( 590)   TGA-ACAAAGGGACTCTA-ATCTGGCAGGAT-ATTC-CA----AAG-C-A

HKLK2.LA0   (7143)   TCCAGTG-TGGCC-CAAGCTCCCGTGTAAACACAGGCACTCTAAACAG--
                     :  :: : :: :: :  ::    :   ::: : : : :    ::: ::
PSE         ( 630)   T-TAGAGATGACCTCTTGC-AAAG-AAAAAGAAATGGAAAAGAAAAAGAA

HKLK2.LA0   (7189)   -G-CAGGATATTTCAAAAGCTT-AGAGATGACCTCCCAGGAGCTGAATGC
                      :  :::: :    ::::     :::::::::::: ::::  ::::  :
PSE         ( 677)   AGAAAGGAAAAAAAAAAAAAAAAAGAGATGACCTCTCAGGCTCTGAGGGG

HKLK2.LA0   (7236)   AAA-GACCTGGCCTCTTTGGGCAAGGAGAATCCTTTACCGCACACTCTCC
                     ::: : ::::   :::::: ::::::  : :::: :   ::::: :::::
PSE         ( 727)   AAACG-CCTGAGGTCTTTGAGCAAGGTCAGTCCTCTGTTGCACAGTCTCC

HKLK2.LA0   (7285)   TTCACAGGGTTATTGTGAGGATCAAATGTGGTCATGTGTGTGAGACACCA
                      ::::::::: ::::::: ::::::::::::::: :::: :::: :::::
PSE         ( 776)   CTCACAGGGTCATTGTGACGATCAAATGTGGTCACGTGTATGAGGCACCA
                                     :                    :::

HKLK2.LA0   (7335)   GCACATGTCTGGCTGTGGAGAGTGACTTCTA--TGTGTGCTAACATTGCT
                     ::::::: :::::: ::: ::::: : : ::  ::: ::::  :: ::::
PSE         ( 826)   GCACATGCCTGGCTCTGGGGAGTGCCGTGTAAGTGTATGCTTGCACTGCT
                     :: : :    :     ::  :      :::  : : : :          :

HKLK2.LA0   (7383)   GAGTGCTAAGAAAGTATTAGGCATGGCT-TTCAGCACTCACAGATGCTCA
                     :: ::::  : : :: : ::: ::   : ::::::::: :::::::::::
PSE         ( 876)   GAATGCTTGGGATGTGTCAGGGAT-TATCTTCAGCACTTACAGATGCTCA
                             ::    :           :      :     :   ::
```

FIGURE 2A

```
HKLK2.LA0      (7432)  TCTAATCCTCACAACATGGCTACAGGG-TGGGCACTACTAGCCTCATTTG
                       ::: :::::::::  :::  :::  ::: :: :::: :::::::::::::
PSE            ( 925)  TCTCATCCTCACAGCATCACTA-TGGGATGGGTATTACTGGCCTCATTTG

HKLK2.LA0      (7481)  ACAGAGGAAAG-GACTGTGGATAAGAAGGGGGTGACCAATAGGTCAGAGT
                       :  :: :::: : :::::: : :::: :: :::::: ::::  ::: : 
PSE            ( 974)  ATGGA-GAAAGTGGCTGTGGCTCAGAAAGGGGGGACCACTAGACCAGGGA

HKLK2.LA0      (7530)  CATTCTGGATGCAAGGGG-CTCCAGAGGACCATGATTAGACATTGTCTGC
                       :: ::::::::  :::: :::::: ::::::::  :  ::    ::::
PSE            (1023)  CACTCTGGATGC-TGGGGACTCCAGA-GACCATGACCACTCACCAACTGC

HKLK2.LA0      (7579)  AGAGAAATT----ATGG-CTGGATGTCTCTGCCCCGGAAAGGG-GGA--T
                       :::::::::    ::: :: :::::: ::: :: ::: :::: :::  :
PSE            (1071)  AGAGAAATTAATTGTGGCCT-GATGTCCCTGTCCTGGAGAGGGTGGAGGT

HKLK2.LA0      (7621)  GCACTTTCCTTGACCCCCTATCTCAGATCTTGACTTTGAG-GTTATCTCA
                       : :: :::  : ::: :::: :: :: ::  :: :  :::: :: : : : :: 
PSE            (1120)  GGACCTTCACTAACCTCCTACCT-TGACCCTCTCTTTTAGGGCTCTTTCT

HKLK2.LA0      (7670)  GACTTCCTCTATGATACCAGGAGCCCATCATAATCTCTCTGTGTCCTCTC
                       ::: ::: : ::: ::: :: :::  :: ::  : : ::: ::  :: ::
PSE            (1169)  GACCTCCACCATGGTACTAGGA-CCC--CATTGTAT-TCTGT-ACC-CT-

HKLK2.LA0      (7720)  CCCTTCCTCAGTCTTACTG-CCCACTCTTCCCAGCTCCATCTCCAGCTGG
                         : :  : :  :: :: :: ::: : :: ::: :: ::  :::::::
PSE            (1212)  --C-T--TGACTC-TA-TGACCCCCACTGCCCA-CTGCA--TCCAGCT--

HKLK2.LA0      (7769)  CCAGGTGTAGCCACAGTACCTAACTCT-TTGCAGAGAACTATAAATGTGT
                          :: ::  :: :  : :: :: :::: :: :  ::  ::    : :::
PSE            (1250)  ---GG-GT--CC-C-CT-CCTATCTCTATT-CCCAG--CTGGCCA-GTGC

HKLK2.LA0      (7818)  A-TCCTACAGGGGAGAAAAAAA-AAAAG-AACTCTGAAAGAGCTGACATT
                       : : :: :::  :      :: :::::::: : :::::::::
PSE            (1287)  AGT-CT-CAGTGCCCACCTGTTTGTCAGTAACTCTGAAGGGGCTGACATT

HKLK2.LA0      (7865)  TTACCGACTTGCAAACACATAAGCTAACCTGCCAG--TTTTGT----GCT
                       :::: ::::::::::::: :::::::::: :  ::::  ::::::    :::
PSE            (1335)  TTACTGACTTGCAAACAAATAAGCTAACTTTCCAGAGTTTTGTGAATGCT

HKLK2.LA0      (7909)  GGTAGAACT-CATGAGACTCCTGGGTCAGAGGCAAAAGATTTTATTACCC
                       :: :: : : ::::::::::::: ::::::::::: : :::: : : :
PSE            (1385)  GGCAG-AGTCCATGAGACTCCTGAGTCAGAGGCAAAGGCTTTTACTGCTC
```

FIGURE 2B

```
HKLK2.LA0   ( 7958)   ACAGCTAAGGAGGCAGCATGAACTTTGTGTTCACATTTGTTCACTTTGCC
                      :::::: :: :: ::::::::  ::  :::::::::: :: ::: :::::
PSE         ( 1434)   ACAGCTTAGCAGACAGCATGAGGTTCATGTTCACATTAGTACACCTTGCC

HKLK2.LA0   ( 8008)   CCCC--AATTCATAT-GGGATGATCAGAGCAGTTC-AGGTGGATG--G-A
                      ::::  :: :: : : ::: ::: :::::::: :: :::::::::  :  
PSE         ( 1484)   CCCCCCAAATCTTGTAGGG-TGACCAGAGCAG-TCTAGGTGGATGCTGTG

HKLK2.LA0   ( 8051)   CA-CAGGGGTTTGTGGCAAAGGTGAGCAACCTAG-GCTTAGAAATCCTCA
                      ::  ::::::::::: ::  :::::: ::::: : : :::: ::::::::
PSE         ( 1532)   CAGAAGGGGTTTGTGCCACTGGTGAGAAACCT-GAGATTAGGAATCCTCA

HKLK2.LA0   ( 8099)   ATCTTATAAGAAGGTACT---AGCAAACTTGTC-CAGTCTTTGTATCTGA
                      ::::::: :   :: ::       :::::: :: : ::: :::::: :::::
PSE         ( 1581)   ATCTTAT-ACTGGG-ACAACTTGCAAACCTG-CTCAGCCTTTGTCTCTGA

HKLK2.LA0   ( 8145)   CGGAGATATTATCTTTATAAT-TGGG-TTGAAAGCAGACCTACTCTGGAG
                       : :::::::::::: :: :: : :: :::::: ::::::::::::::::
PSE         ( 1628)   TGAAGATATTATCTTCATGATCTTGGATTGAAAACAGACCTACTCTGGAG

HKLK2.LA0   ( 8193)   GAACATATTGTATTTATTGTCCT-GAACAGTAAACAAATCTGCTGTAAAA
                      :::::::::::::  :::::::: : :::::::::::::::: :::  ::
PSE         ( 1678)   GAACATATTGTATCGATTGTCCTTG-ACAGTAAACAAATCTGTTGT--AA

HKLK2.LA0   ( 8242)   TAGACGTTAACTTTATTATCTAAGG-CAGTAAGCAAACCTAGATCTGAAG
                       :::: ::: ::::::::::: ::: :::::::::: ::: :::::: ::
PSE         ( 1725)   GAGACATTATCTTTATTATCT-AGGACAGTAAGCAAGCCTGGATCTG-AG

HKLK2.LA0   ( 8291)   -GCGATACCATCTTGCAAGGCTATCTGCTGTACAAATATGCTTGAAAAGA
                       : :::: :::::::::::: :  ::::: :::::: :: :::::::  :
PSE         ( 1773)   AGAGATATCATCTTGCAAGGATGCCTGCTTTACAAACATCCTTGAAACAA

HKLK2.LA0   ( 8340)   TGGTCCAGAAAAGAAAACGGTATTATTGCCTTTGCTCAGAAGACACACAG
                         ::::::::: :::: ::: ::   : :::::::::::::::::::::
PSE         ( 1823)   CAATCCAGAAAA-AAAAAGGTGTTGCTGTCTTTGCTCAGAAGACACACAG

HKLK2.LA0   ( 8390)   AAACATAAGAGAACCATGGAAAATTGTCTCCCAACACTGTTCACCCAGAG
                      : :: : : ::::::::::: ::::: :::::::: ::::::: ::::::
PSE         ( 1872)   ATACGTGACAGAACCATGGAGAATTGCCTCCCAACGCTGTTCAGCCAGAG

HKLK2.LA0   ( 8440)   CCTTCCACTCTTGTCTGCAGGACAGTCTTAACATCCCATCATTAG-T-GT
                      :::::::: ::::::::::::::::::: ::: : ::: :::::  :  :
PSE         ( 1922)   CCTTCCACCCTTGTCTGCAGGACAGTCTCAACGTTCCACCATTAAATACT
```

FIGURE 2C

```
HKLK2.LA0       (8488)    --GTCTACCACATCTGGCTTCACCGTGCCTAACCAAGATTTCTAGGTCCA
                             :::: ::::::  :::::    ::::::::::::  ::::::::::
PSE             (1972)    TCTTCTATCACATCCTGCTTCTTTATGCCTAACCAAG-GTTCTAGGTCCC
                                :        ::    : :   :      : :   :: :::   :

HKLK2.LA0       (8536)    GTTCCCCACCATGTTTGGCAGTGCCCCACTGCCAACCCCAGAATAAGGGA
                          : :  : ::  ::: ::::::  : :::::::::: :::::::::::: :
PSE             (2021)    GAT--CGACTGTGTCTGGCAGCACTCCACTGCCAAACCCAGAATAAGGCA
                                ::   :   :: :   :      ::              :   :

HKLK2.LA0       (8586)    GTGCTCAGAATTCCGA
                          : :::::: :: ::::
PSE             (2069)    GCGCTCAGGATCCCGA
                          :            : :
```

FIGURE 2D

09875228.050501

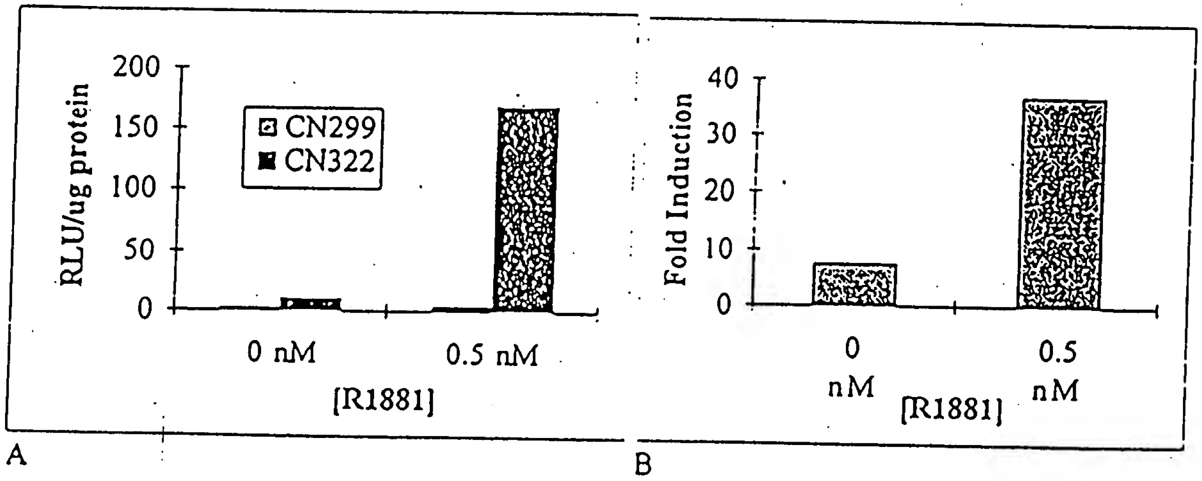

A
RLU/ug protein
200
150
100
50
0
☐ CN299
■ CN322
0 nM
0.5 nM
[R1881]
B
Fold Induction
40
30
20
10
0
0
nM
0.5
nM
[R1881]

FIGURE 3

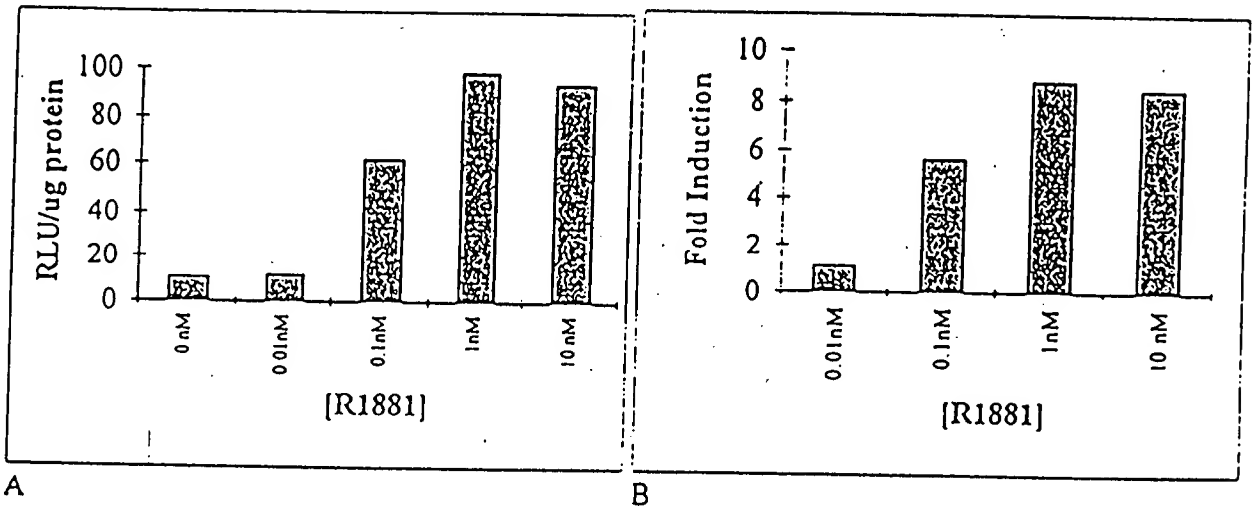

RLU/ug protein
100
80
60
40
20
0
0 nM
0.01nM
0.1nM
1nM
10 nM
[R1881]
A
Fold Induction
10
8
6
4
2
0
0.01nM
0.1nM
1nM
10 nM
[R1881]
B

FIGURE 4

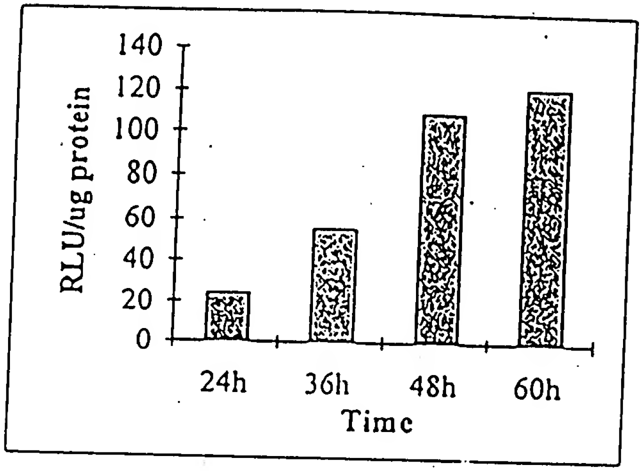


FIGURE 5

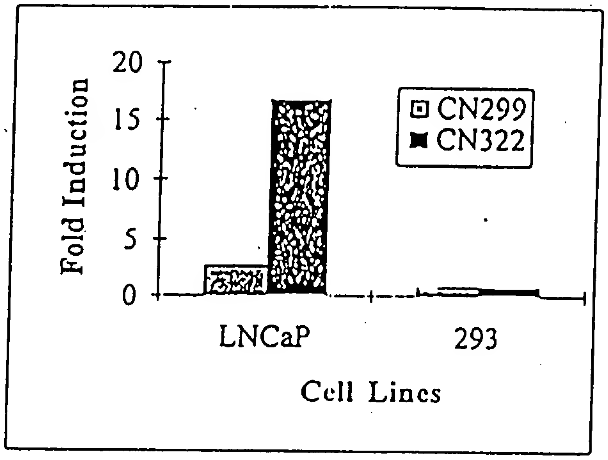


FIGURE 6

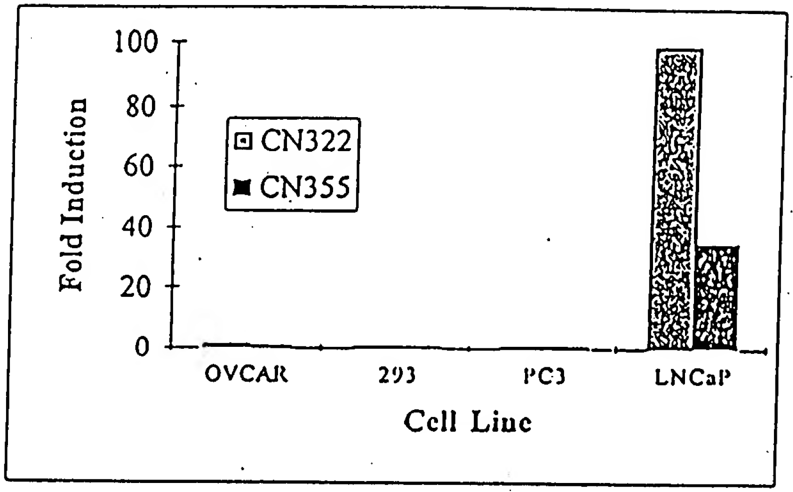

100
80
60
40
20
0
Fold Induction
☐ CN322
■ CN355
OVCAR
293
PC3
LNCaP
Cell Line

FIGURE 7

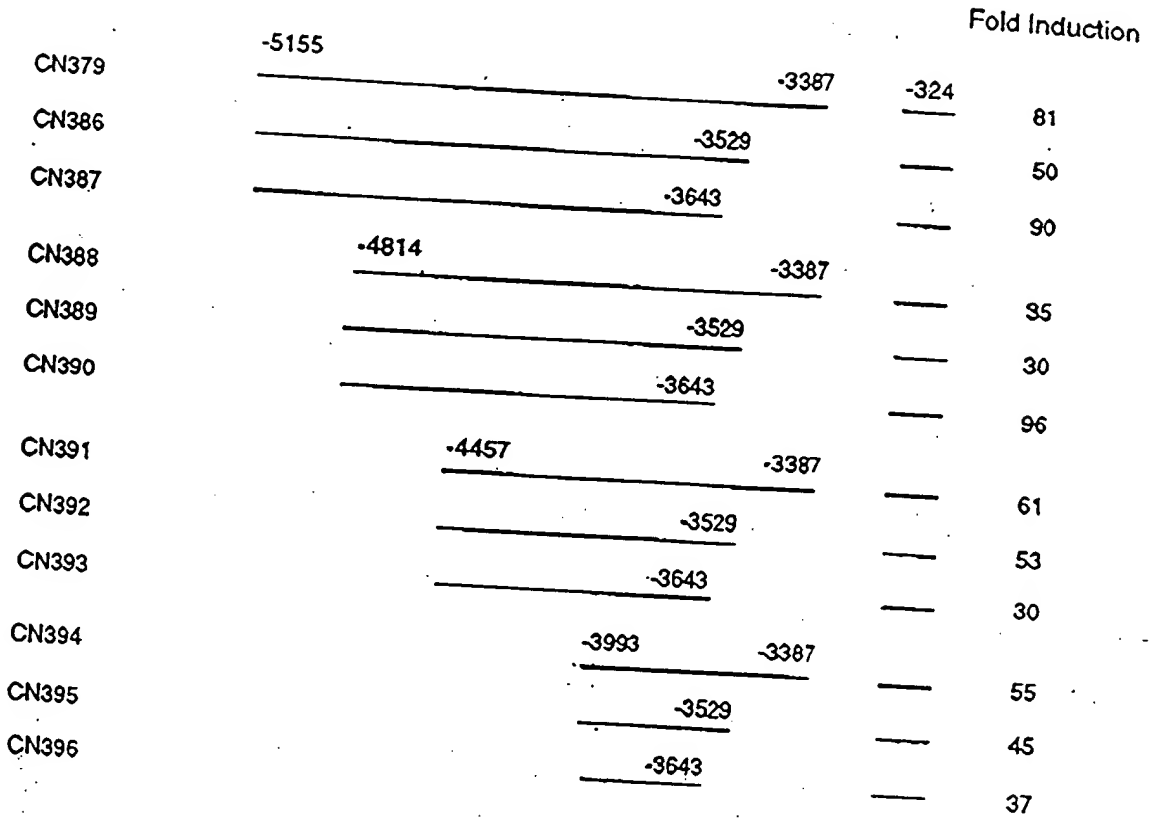

Fold Induction
CN379
-5155
-3387
-324
81
CN386
-3529
50
CN387
-3643
90
CN388
-4814
-3387
CN389
-3529
35
CN390
-3643
30
96
CN391
-4457
-3387
CN392
-3529
61
CN393
-3643
53
30
CN394
-3993
-3387
CN395
-3529
55
CN396
-3643
45
37

FIGURE 8

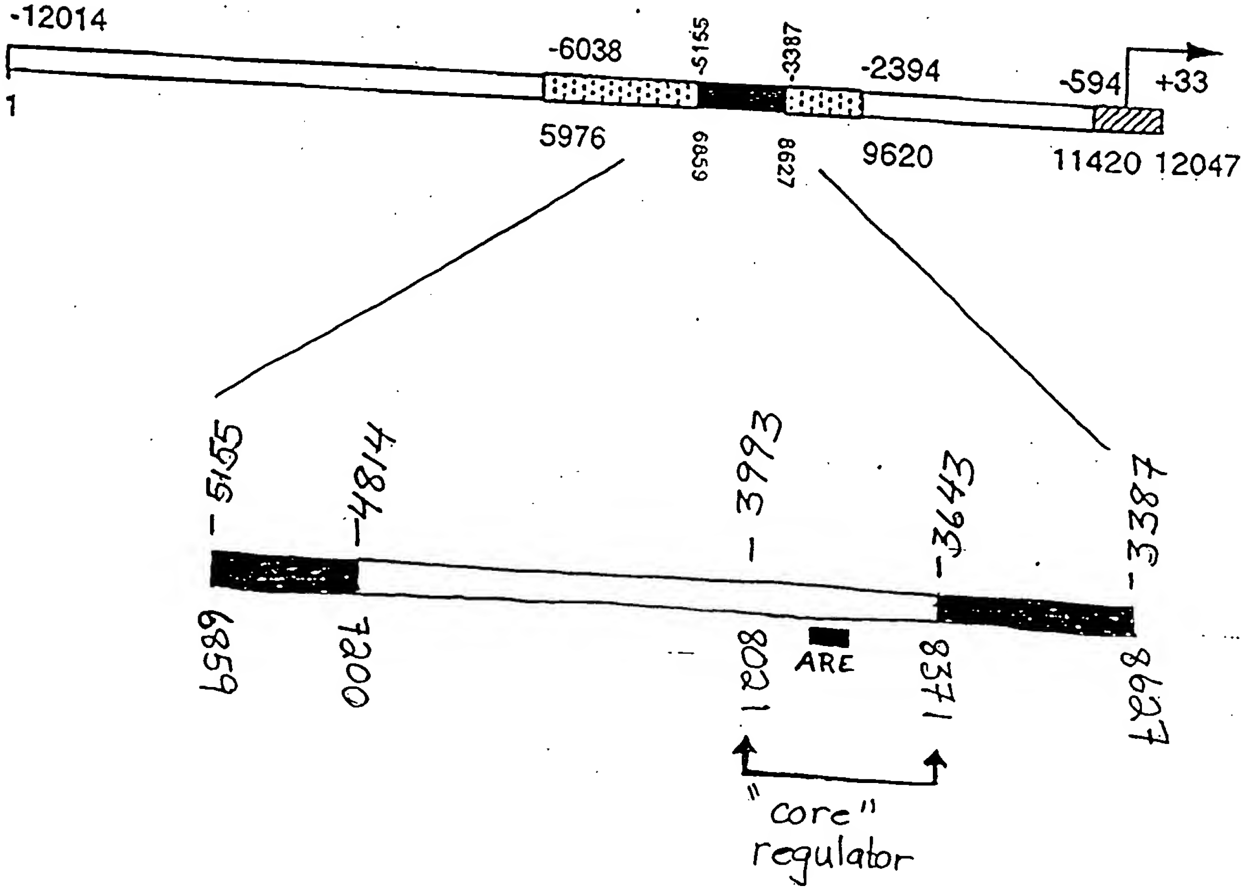

-12014
-6038
-5155
-3387
-2394
-594
+33
1
5976
6859
8627
9620
11420
12047
-5155
-4814
-3993
-3643
-3387
6859
7200
8021
ARE
8371
8627
"core"
regulator

FIGURE 9

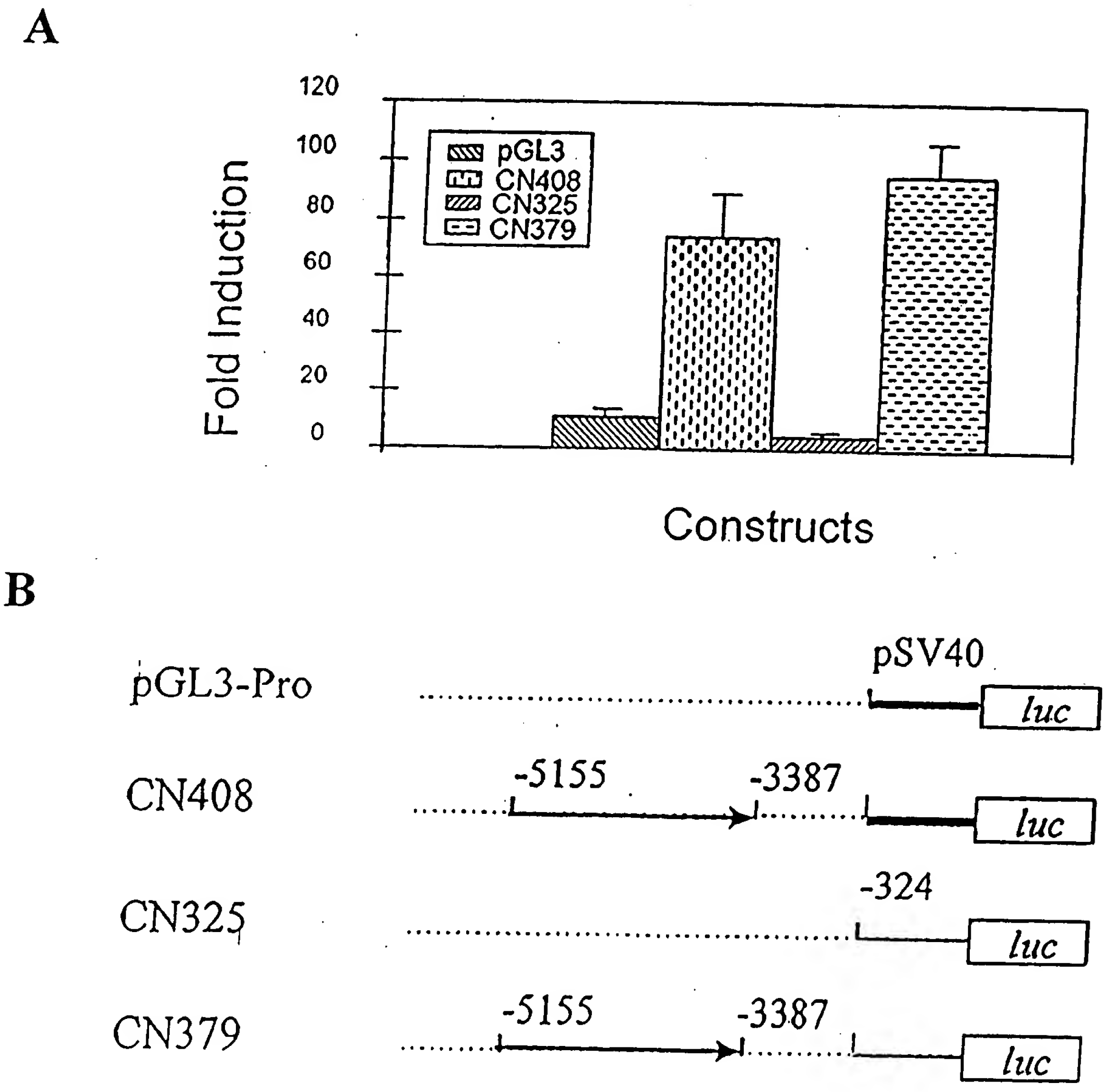

A
Fold Induction
120
100
80
60
40
20
0
pGL3
CN408
CN325
CN379
Constructs
B
pGL3-Pro
CN408
CN325
CN379
pSV40
-5155
-3387
-324
-5155
-3387
luc
luc
luc
luc

FIGURE 10

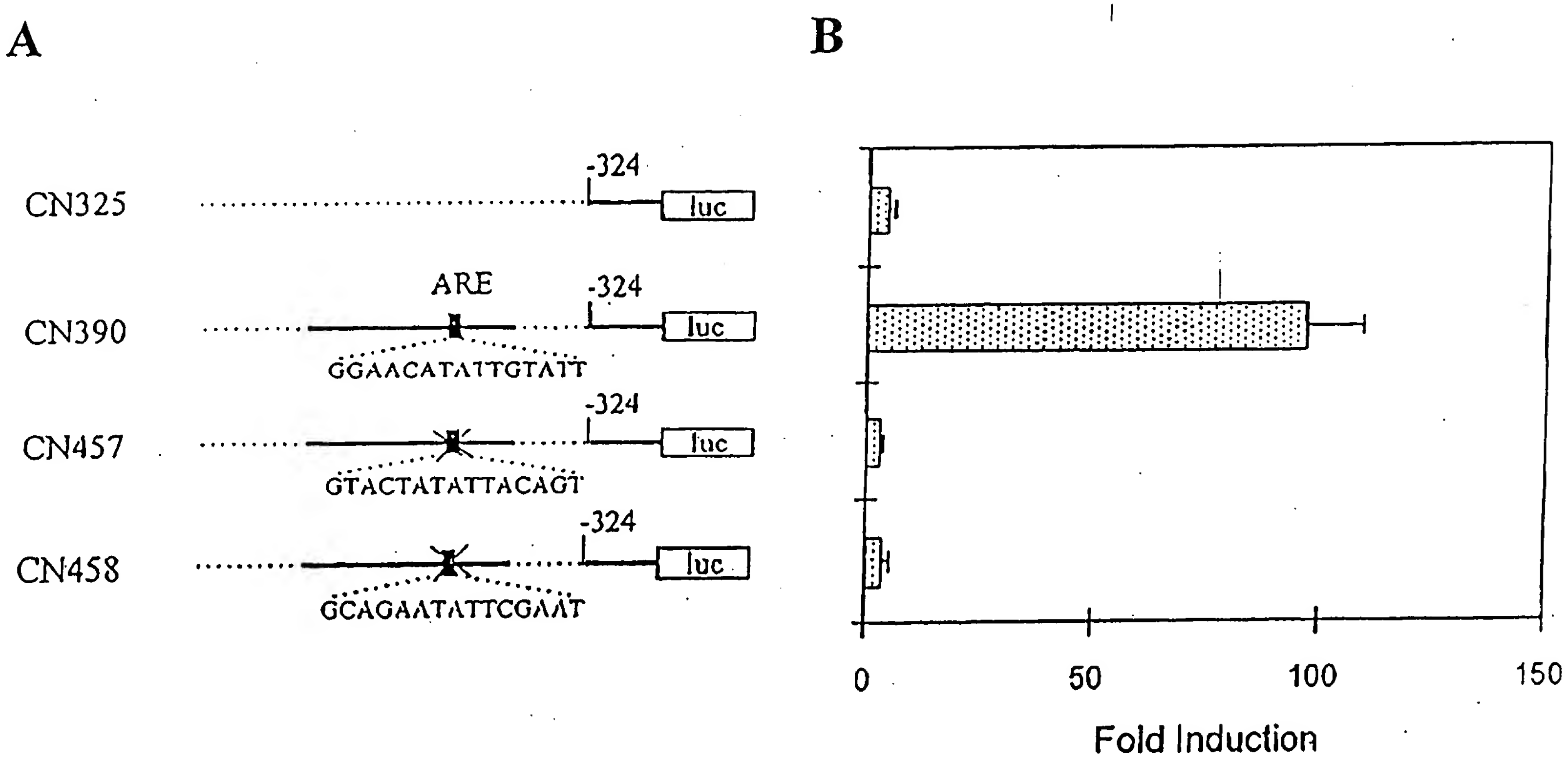

A
B
CN325
CN390
CN457
CN458
-324
-324
-324
-324
luc
luc
luc
luc
ARE
GGAACATATTGTATT
GTACTATATTACAGT
GCAGAATATTCGAAT
0
50
100
150
Fold Induction

FIGURE 11

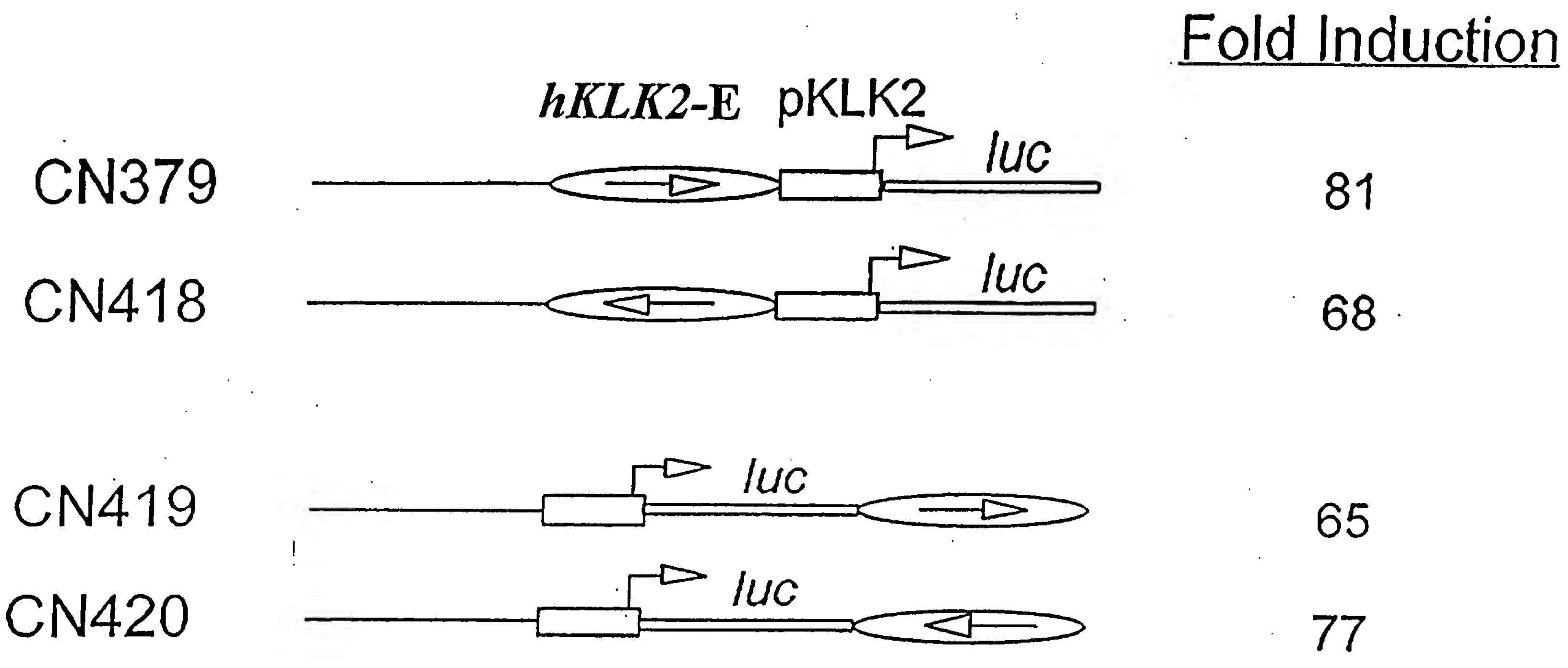

Fold Induction
hKLK2-E
pKLK2
luc
CN379
81
luc
CN418
68
luc
CN419
65
luc
CN420
77

FIGURE 12

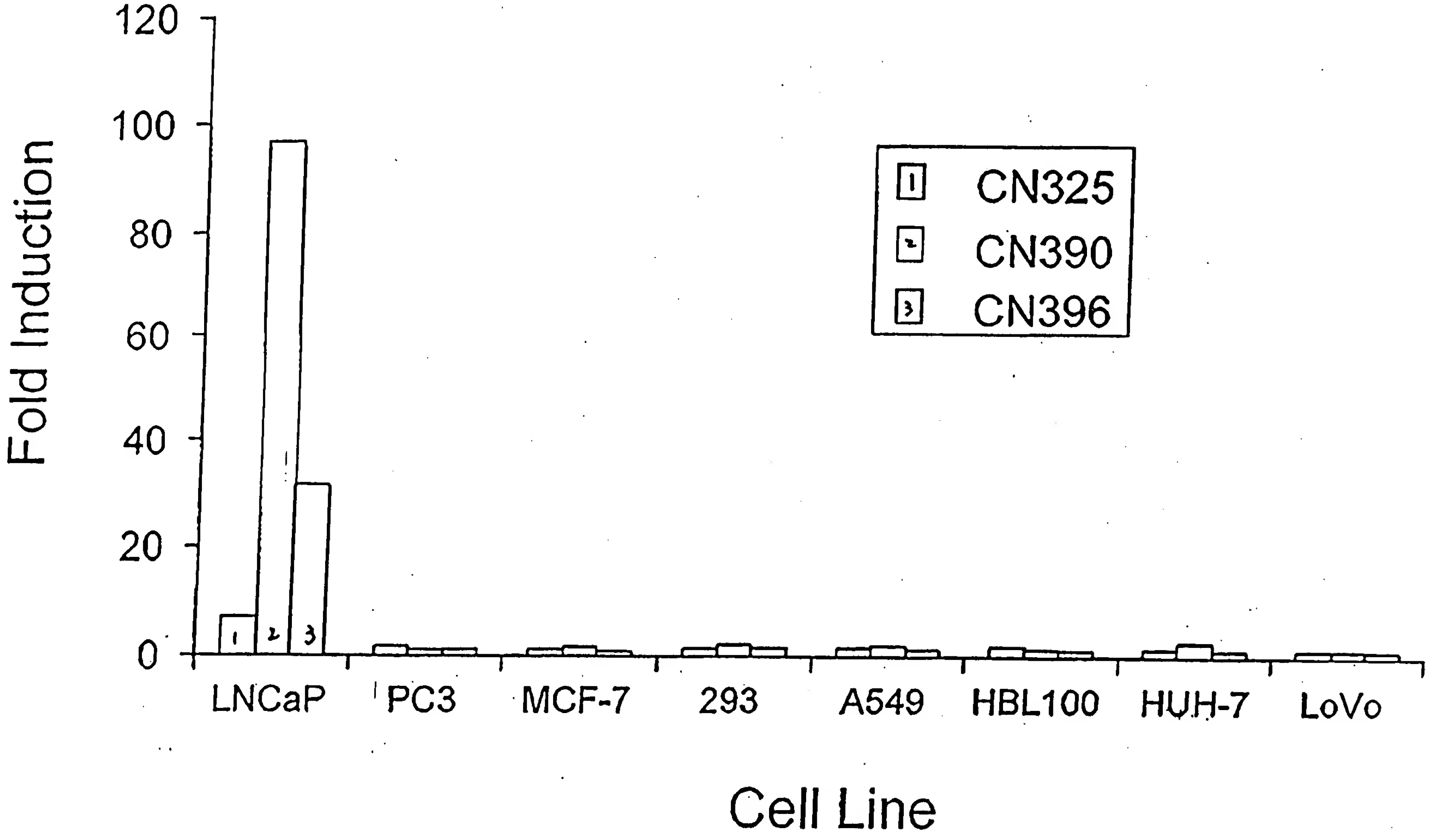

Fold Induction
120
100
80
60
40
20
0
1
2
3
LNCaP
PC3
MCF-7
293
A549
HBL100
HUH-7
LoVo
Cell Line
1 CN325
2 CN390
3 CN396

FIGURE 13

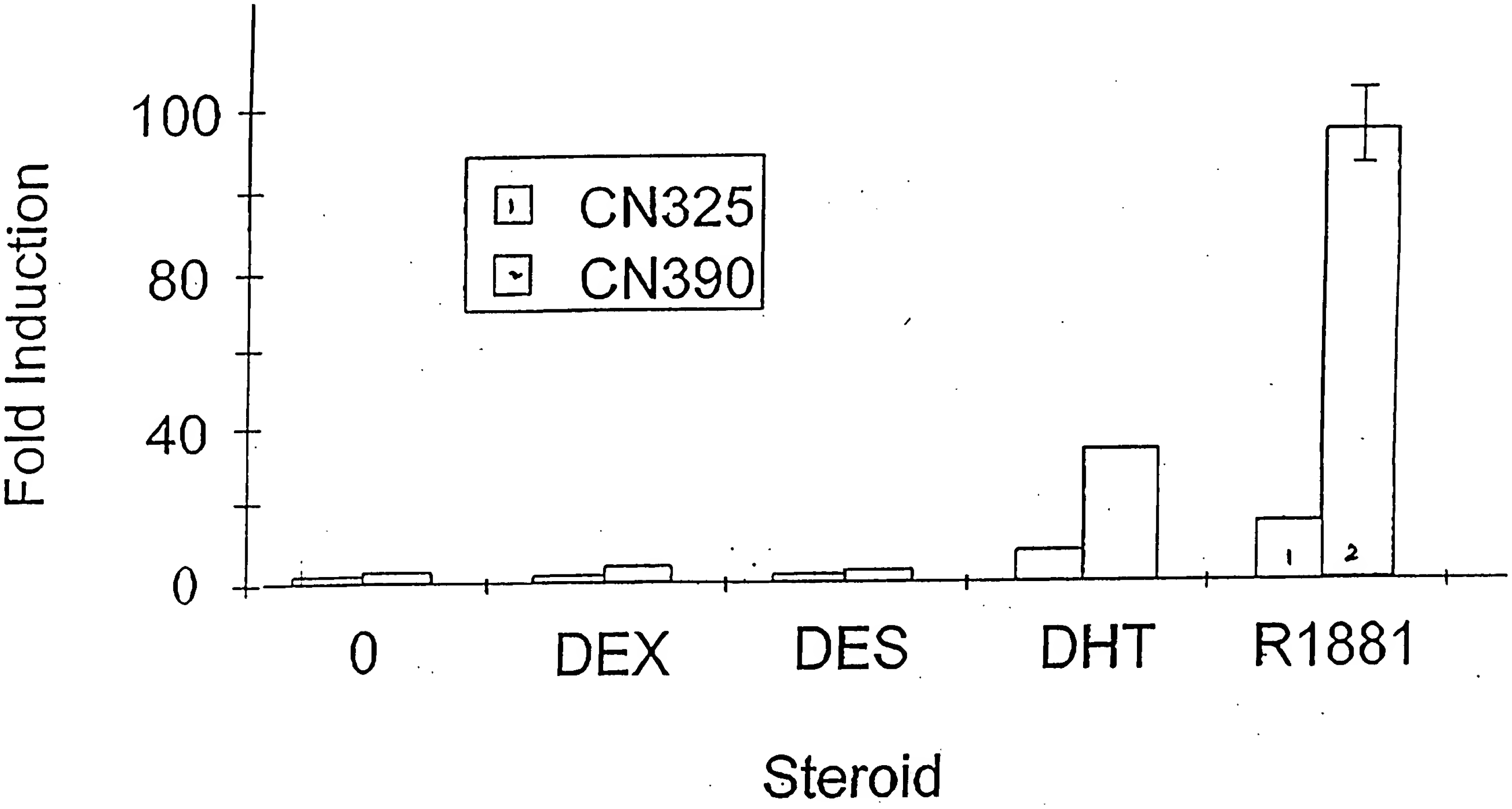

Fold Induction
100
80
40
0
CN325
CN390
1
2
0
DEX
DES
DHT
R1881
Steroid

FIGURE 14

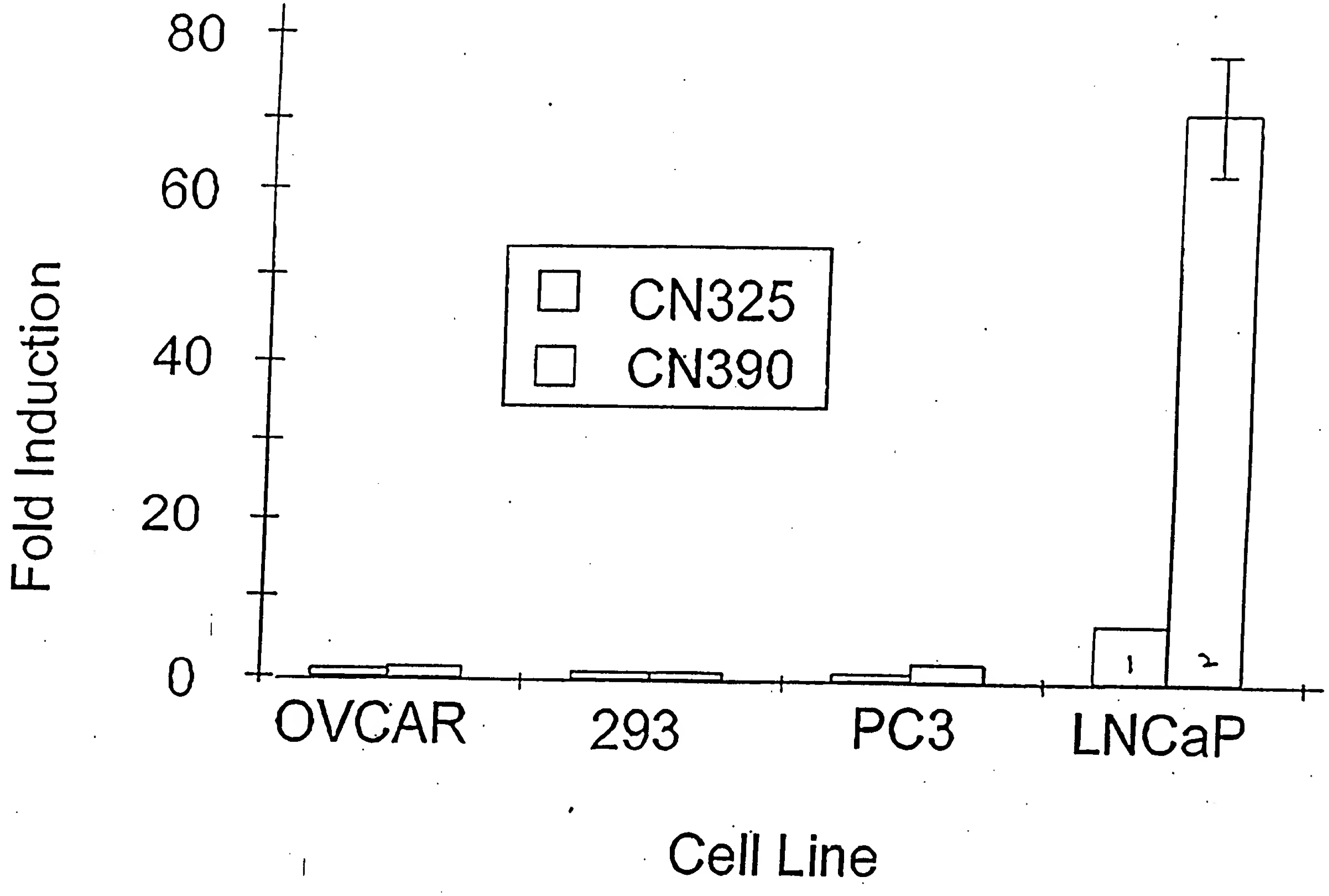

80
60
40
20
0
Fold Induction
CN325
CN390
1
2
OVCAR
293
PC3
LNCaP
Cell Line

FIGURE 15

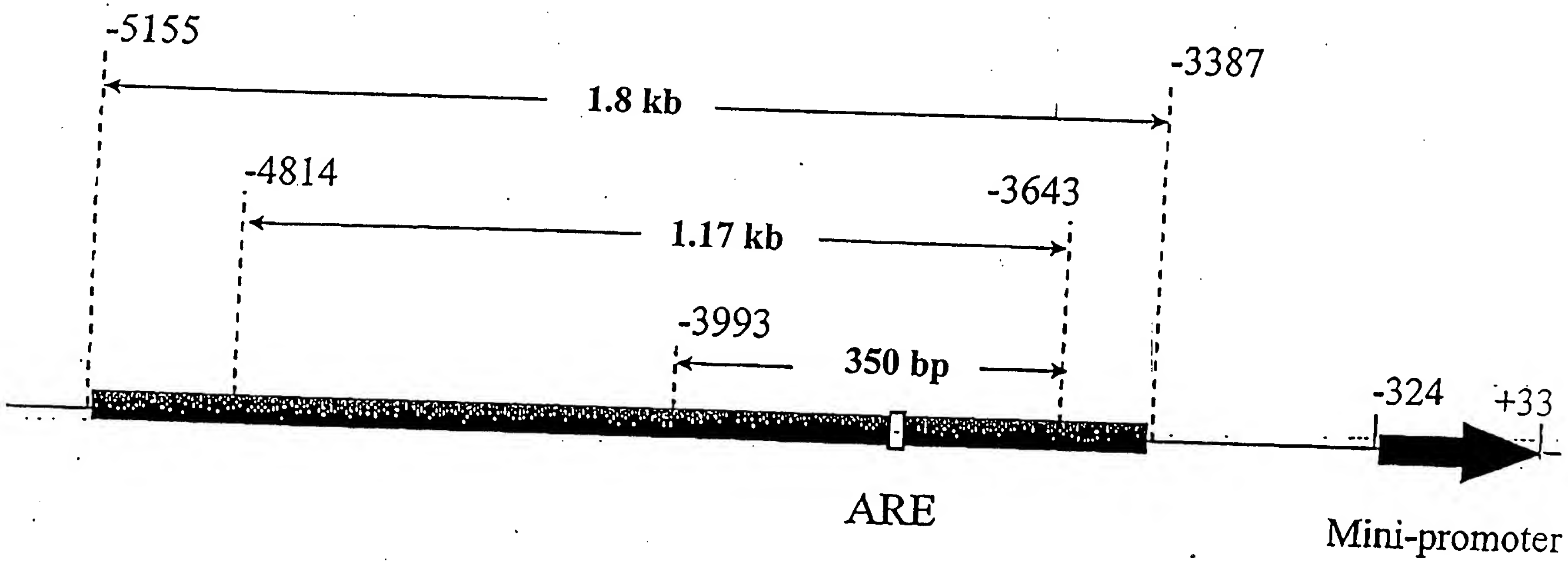

-5155
1.8 kb
-3387
-4814
1.17 kb
-3643
-3993
350 bp
-324
+33
ARE
Mini-promoter

FIGURE 16

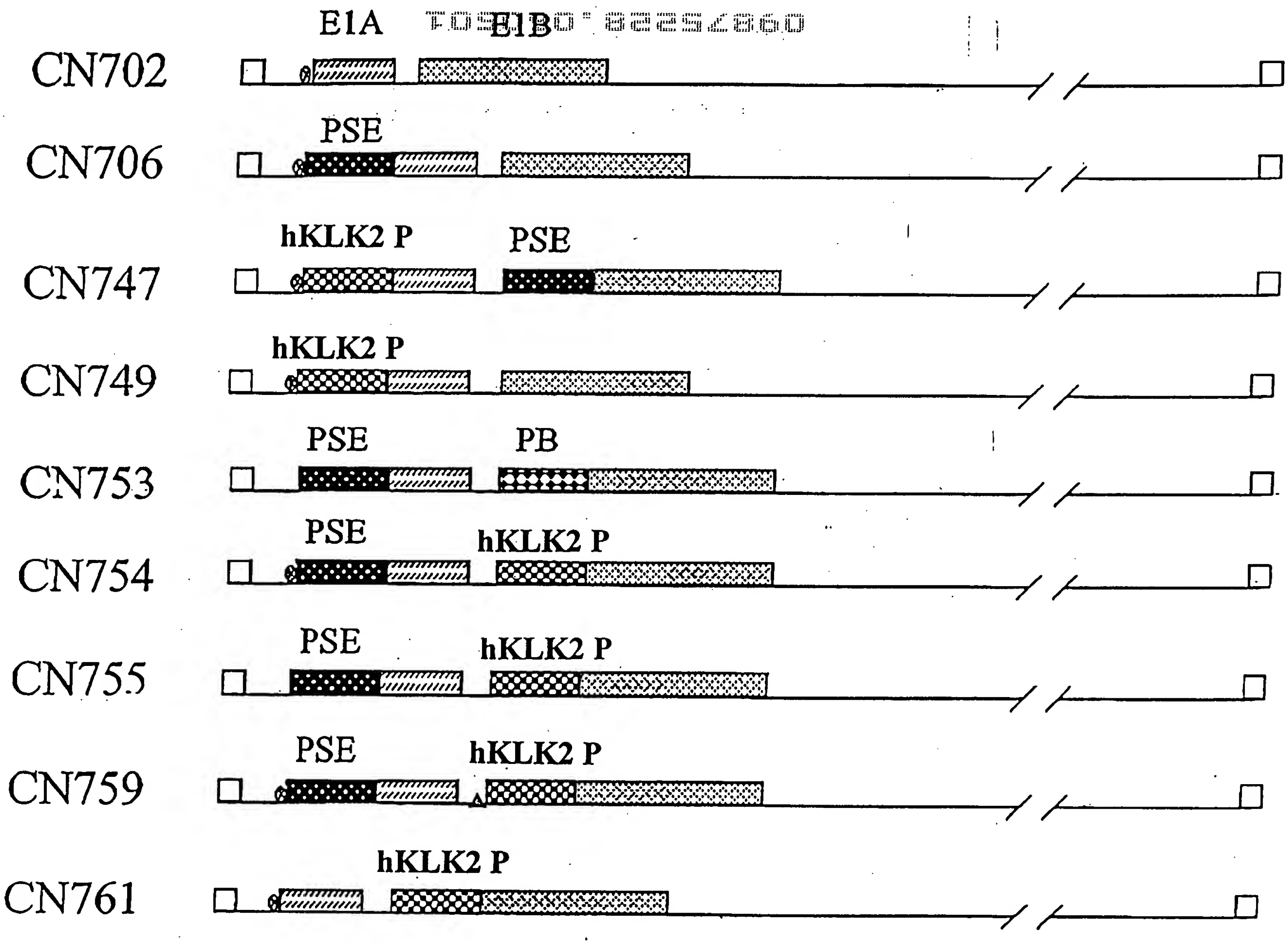

E1A
E1B
CN702
PSE
CN706
hKLK2 P
PSE
CN747
hKLK2 P
CN749
PSE
PB
CN753
PSE
hKLK2 P
CN754
PSE
hKLK2 P
CN755
PSE
hKLK2 P
CN759
hKLK2 P
CN761

FIGURE 17A

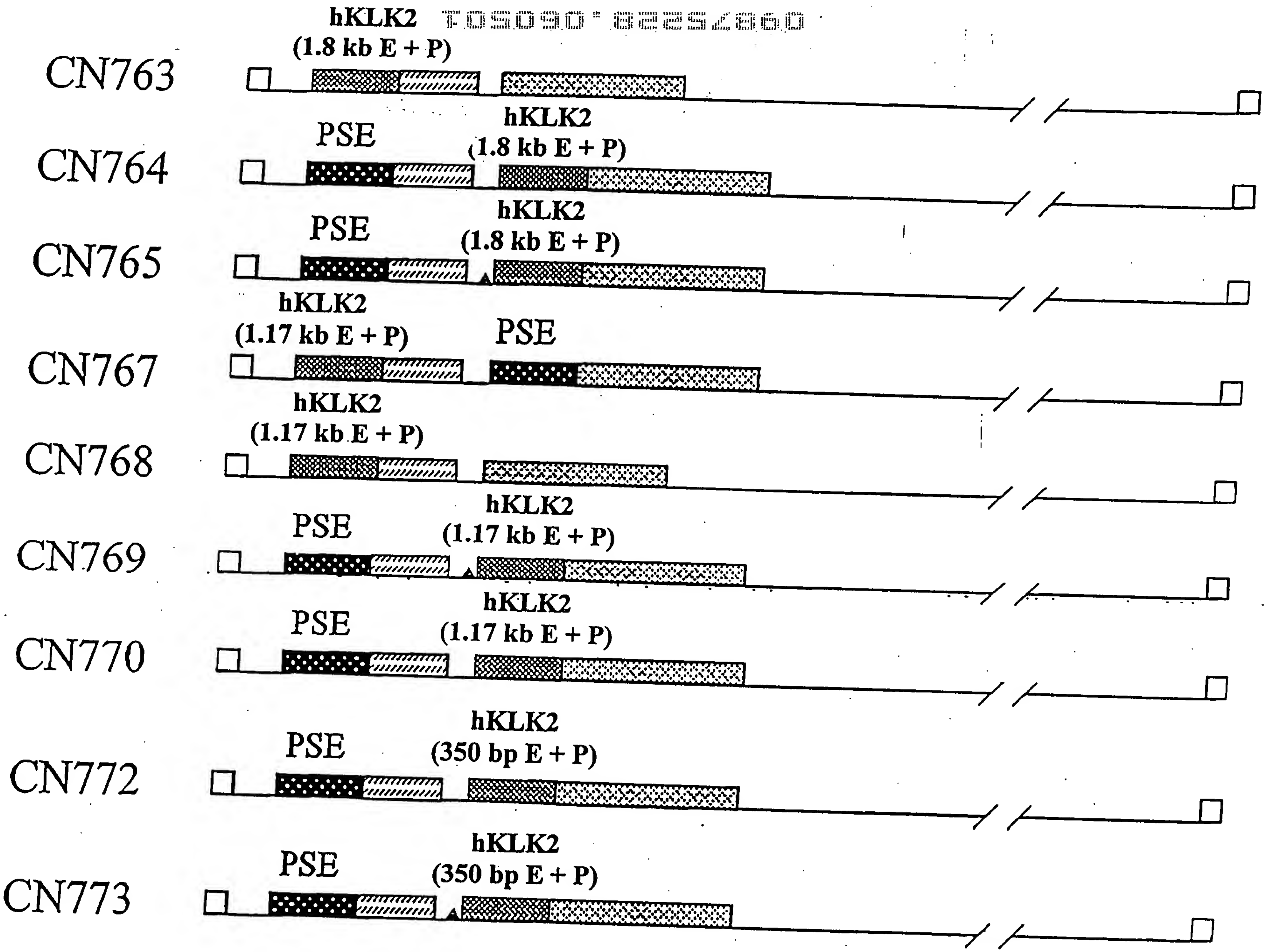

CN763
hKLK2
(1.8 kb E + P)
CN764
PSE
hKLK2
(1.8 kb E + P)
CN765
PSE
hKLK2
(1.8 kb E + P)
CN767
hKLK2
(1.17 kb E + P)
PSE
CN768
hKLK2
(1.17 kb E + P)
CN769
PSE
hKLK2
(1.17 kb E + P)
CN770
PSE
hKLK2
(1.17 kb E + P)
CN772
PSE
hKLK2
(350 bp E + P)
CN773
PSE
hKLK2
(350 bp E + P)

FIGURE 17B

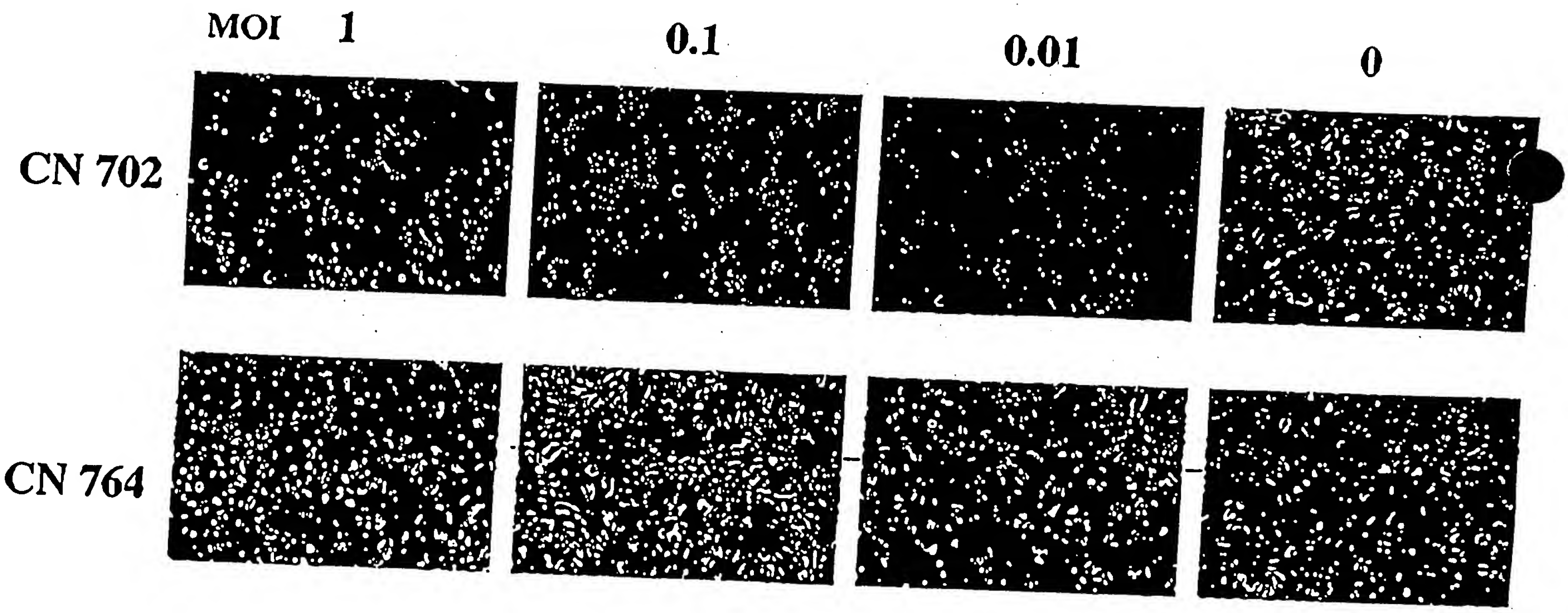


FIGURE 18

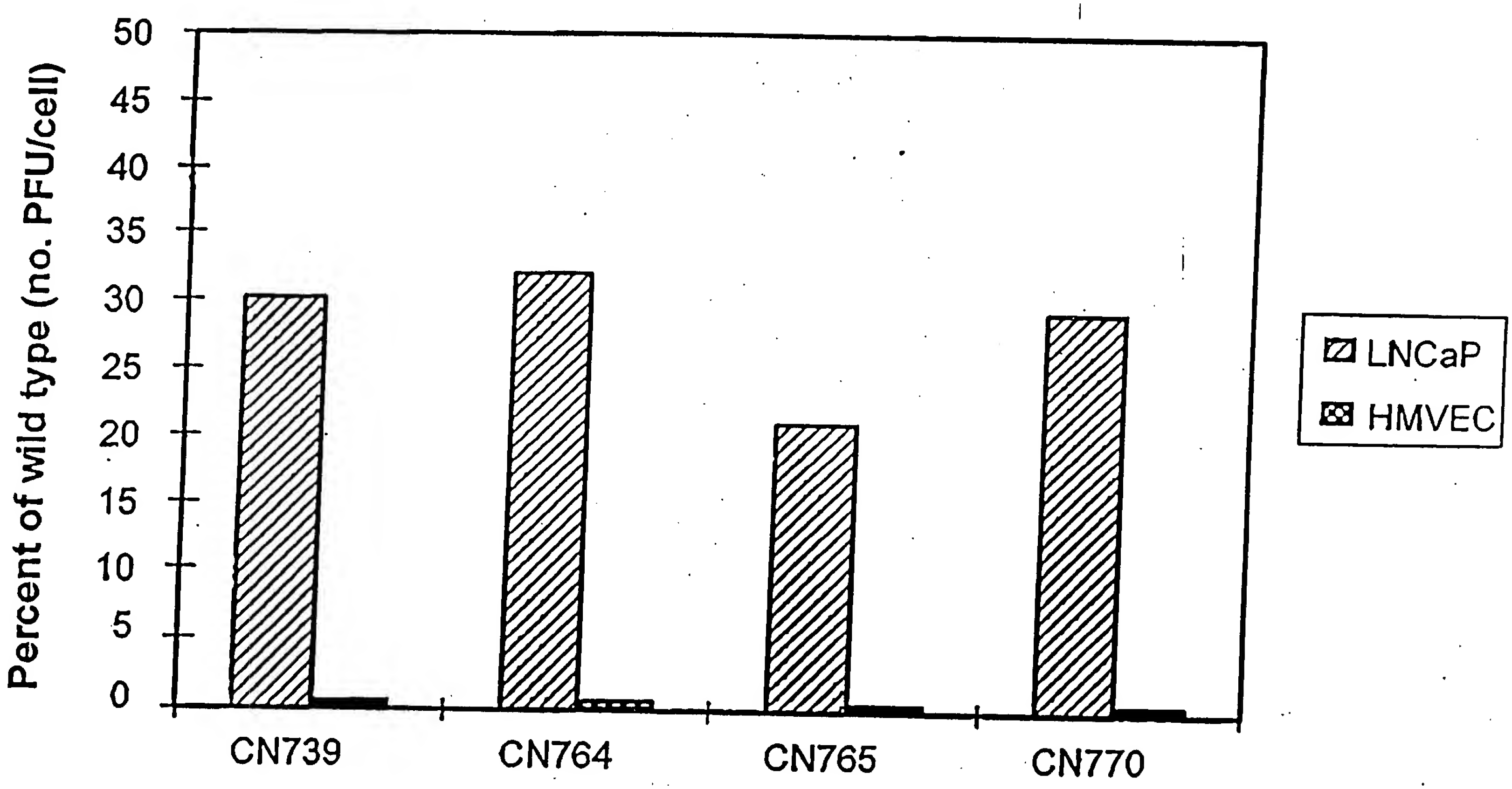

Percent of wild type (no. PFU/cell)
50
45
40
35
30
25
20
15
10
5
0
CN739
CN764
CN765
CN770
▨ LNCaP
▩ HMVEC

FIGURE 19

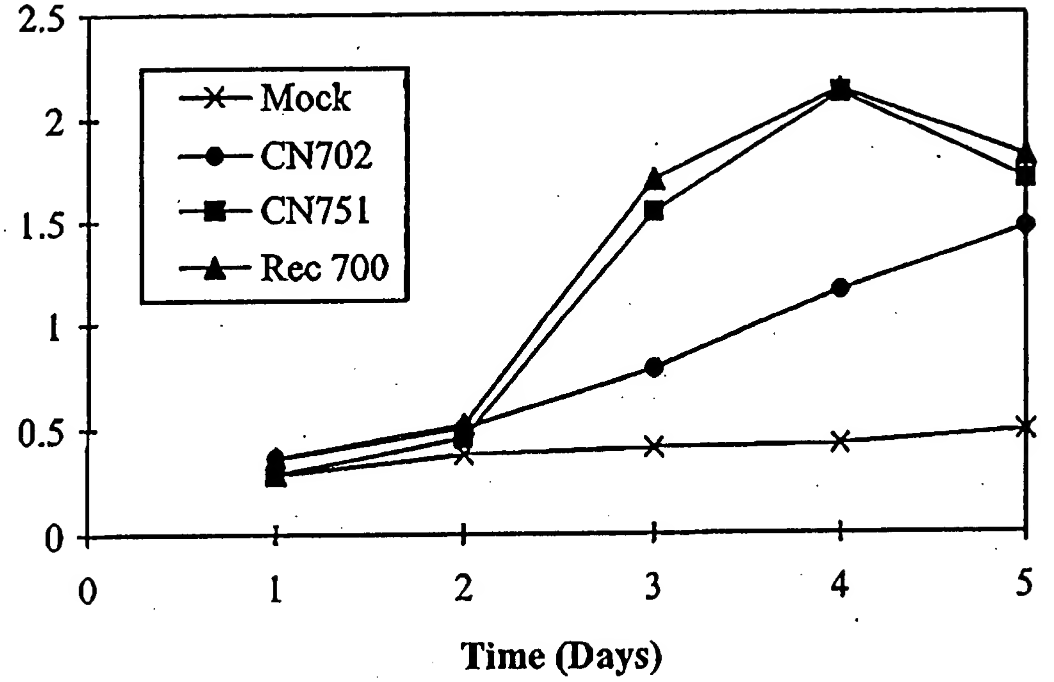


FIGURE 20

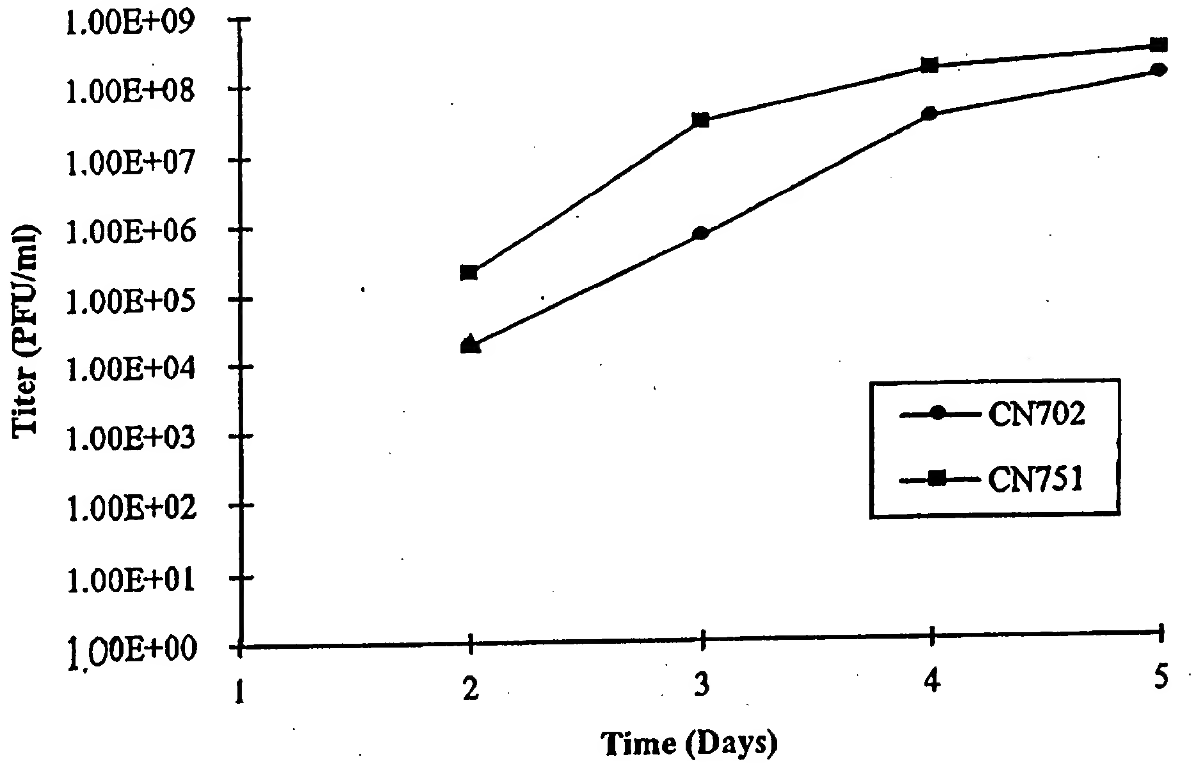

Titer (PFU/ml)
1.00E+09
1.00E+08
1.00E+07
1.00E+06
1.00E+05
1.00E+04
1.00E+03
1.00E+02
1.00E+01
1.00E+00
1
2
3
4
5
Time (Days)
CN702
CN751

FIGURE 21

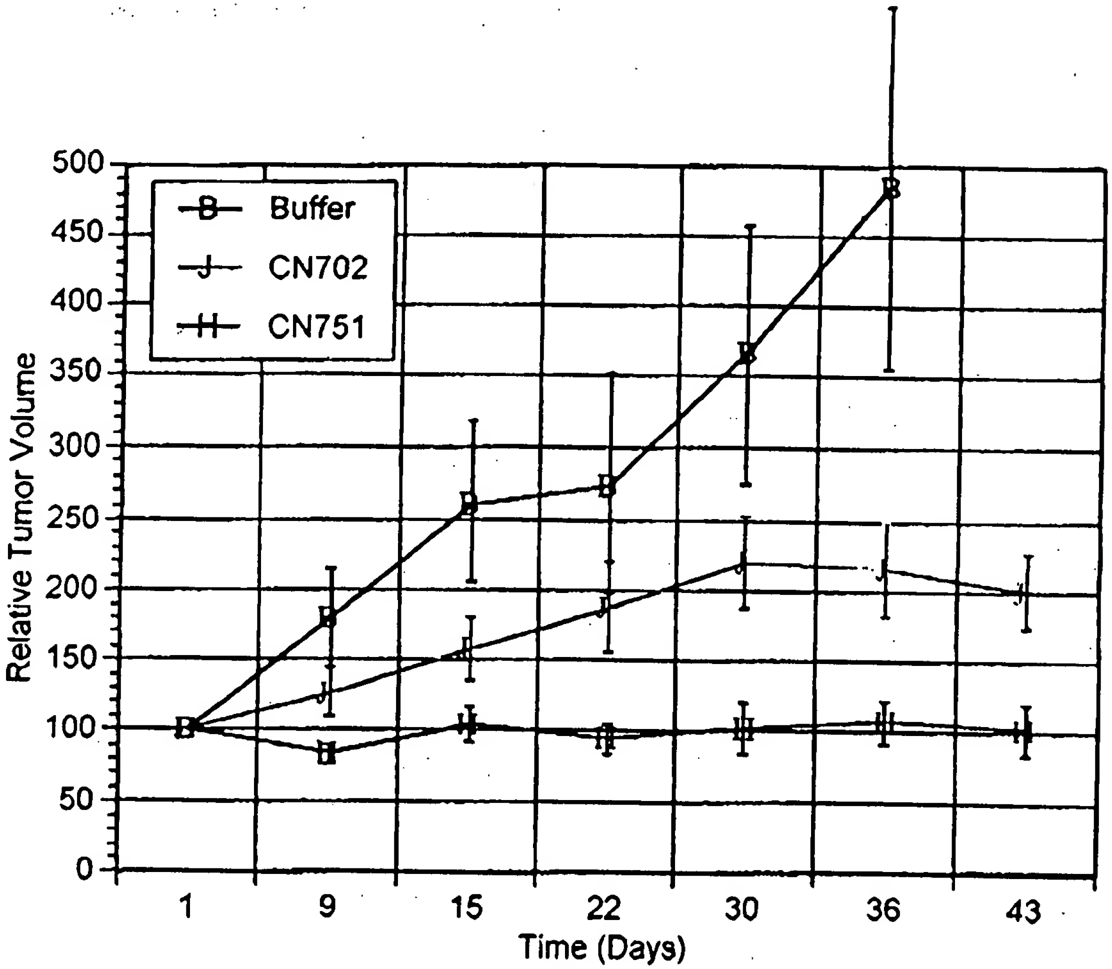

Buffer
CN702
CN751
Relative Tumor Volume
500
450
400
350
300
250
200
150
100
50
0
1
9
15
22
30
36
43
Time (Days)

FIGURE 22

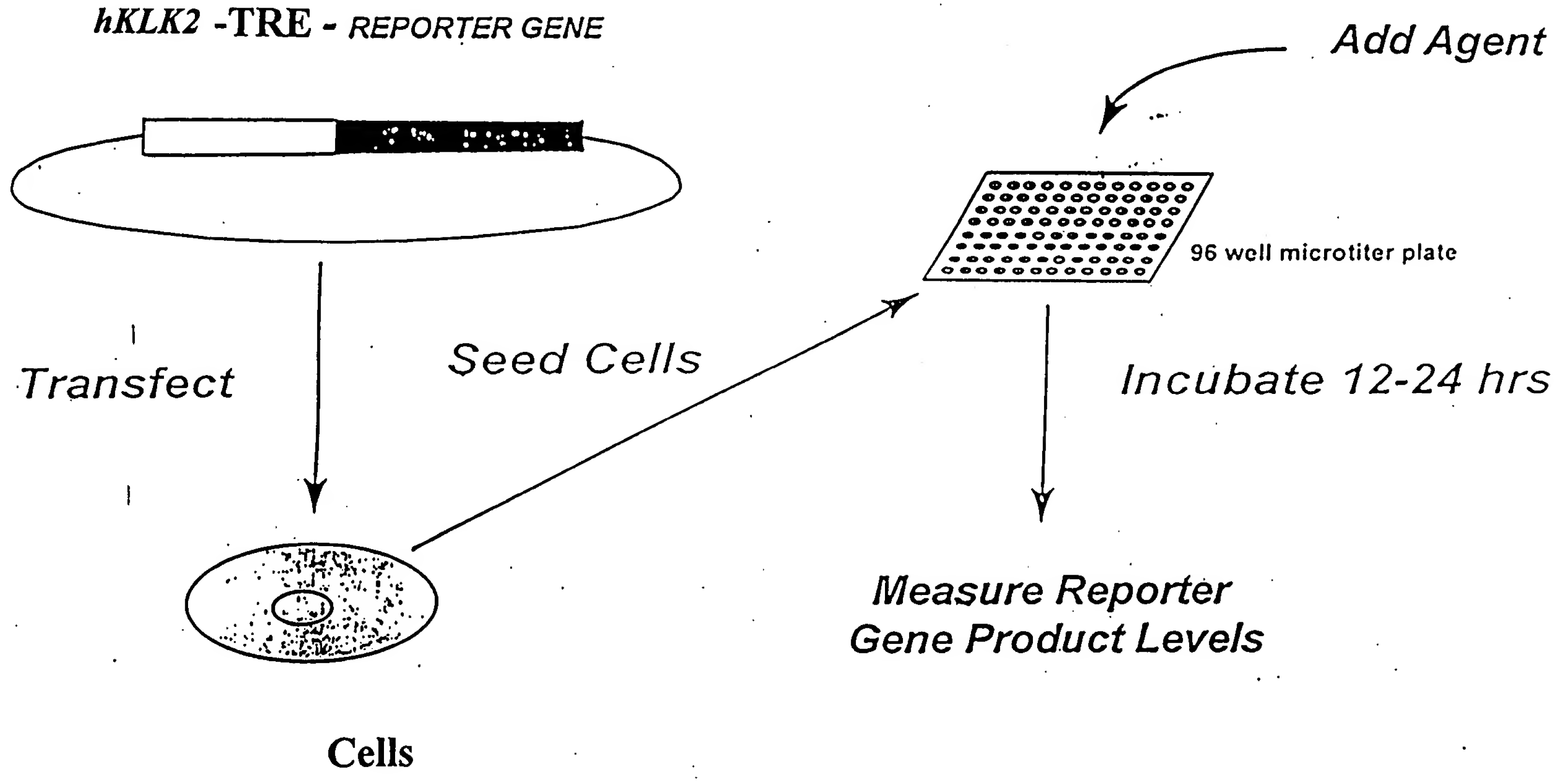

hKLK2 -TRE - REPORTER GENE
Add Agent
96 well microtiter plate
Transfect
Seed Cells
Incubate 12-24 hrs
Measure Reporter Gene Product Levels
Cells

FIGURE 23A

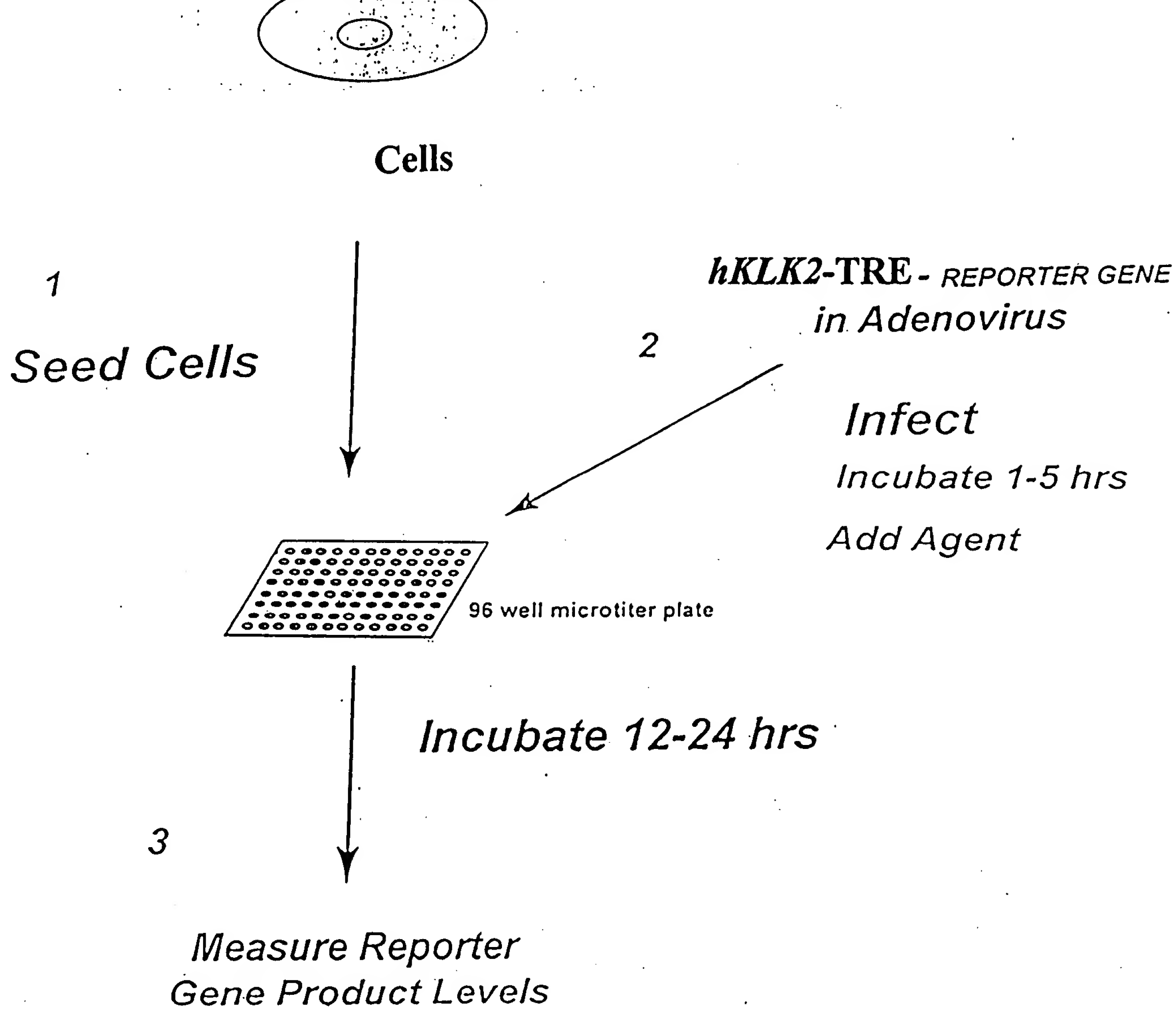

Cells
1
Seed Cells
2
hKLK2-TRE - REPORTER GENE
in Adenovirus
Infect
Incubate 1-5 hrs
Add Agent
96 well microtiter plate
Incubate 12-24 hrs
3
Measure Reporter
Gene Product Levels

FIGURE 23B

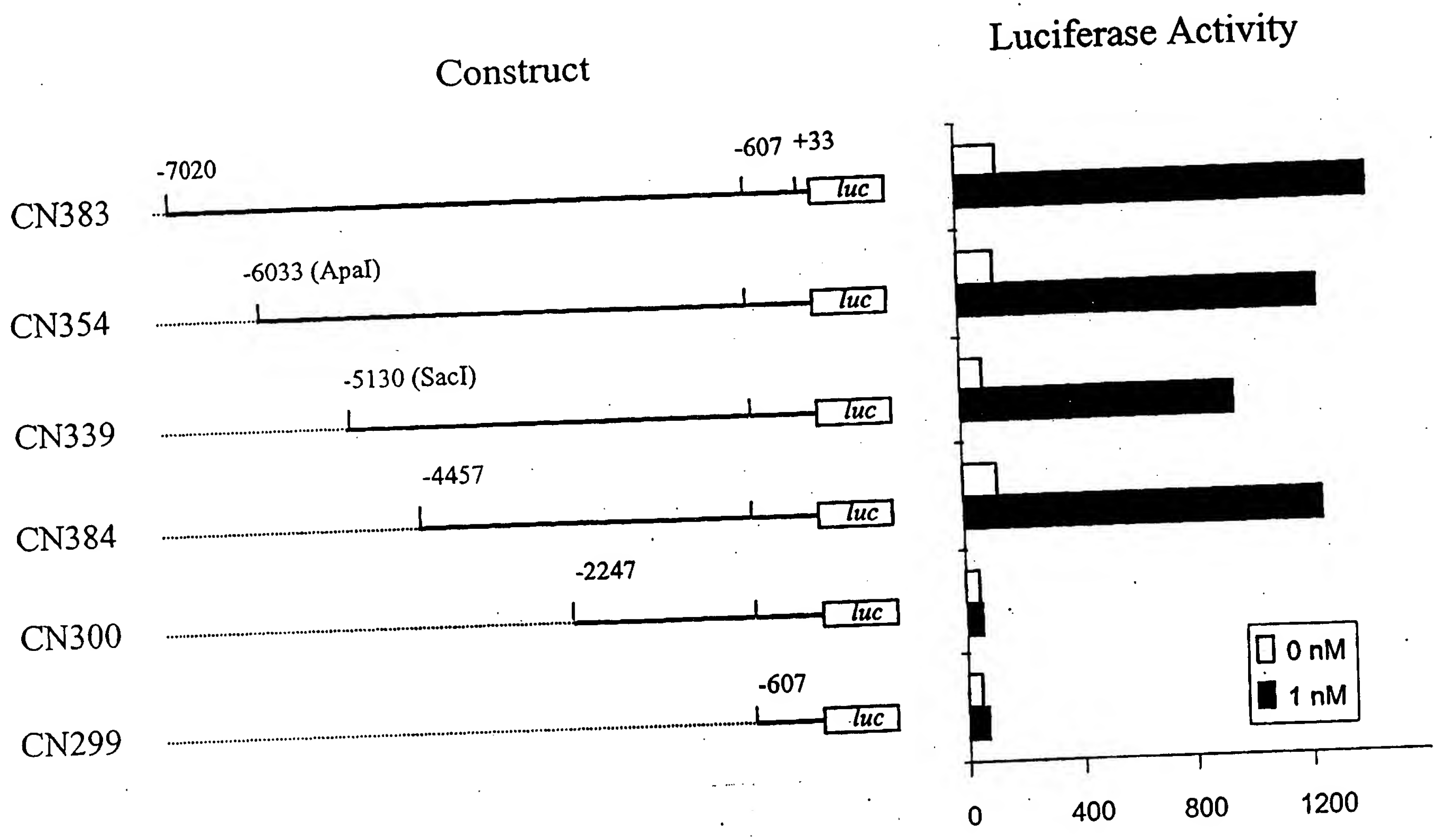

Construct
Luciferase Activity
CN383
CN354
CN339
CN384
CN300
CN299
-7020
-607
+33
-6033 (ApaI)
-5130 (SacI)
-4457
-2247
-607
luc
0 nM
1 nM
0
400
800
1200

FIGURE 24A

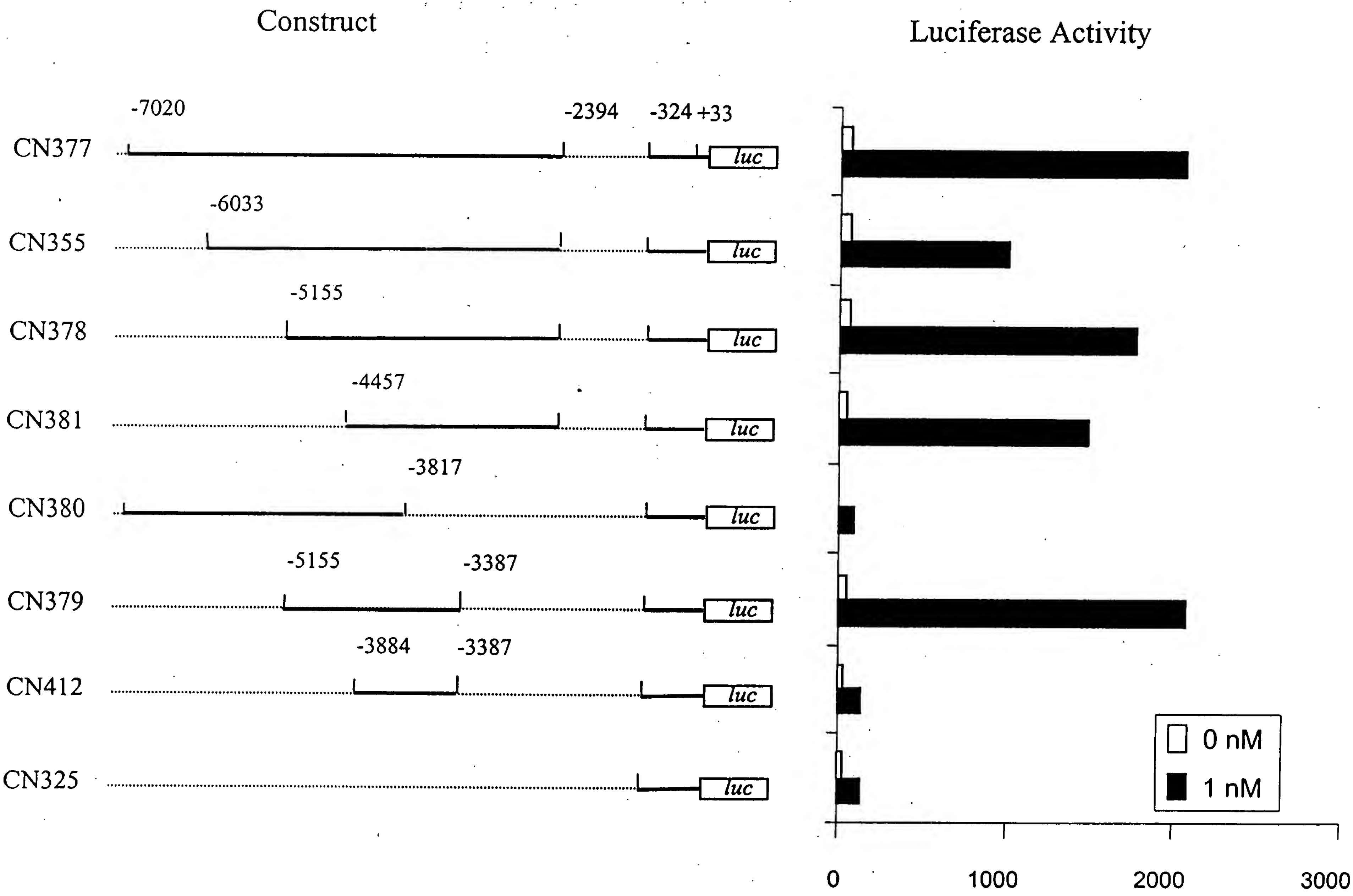
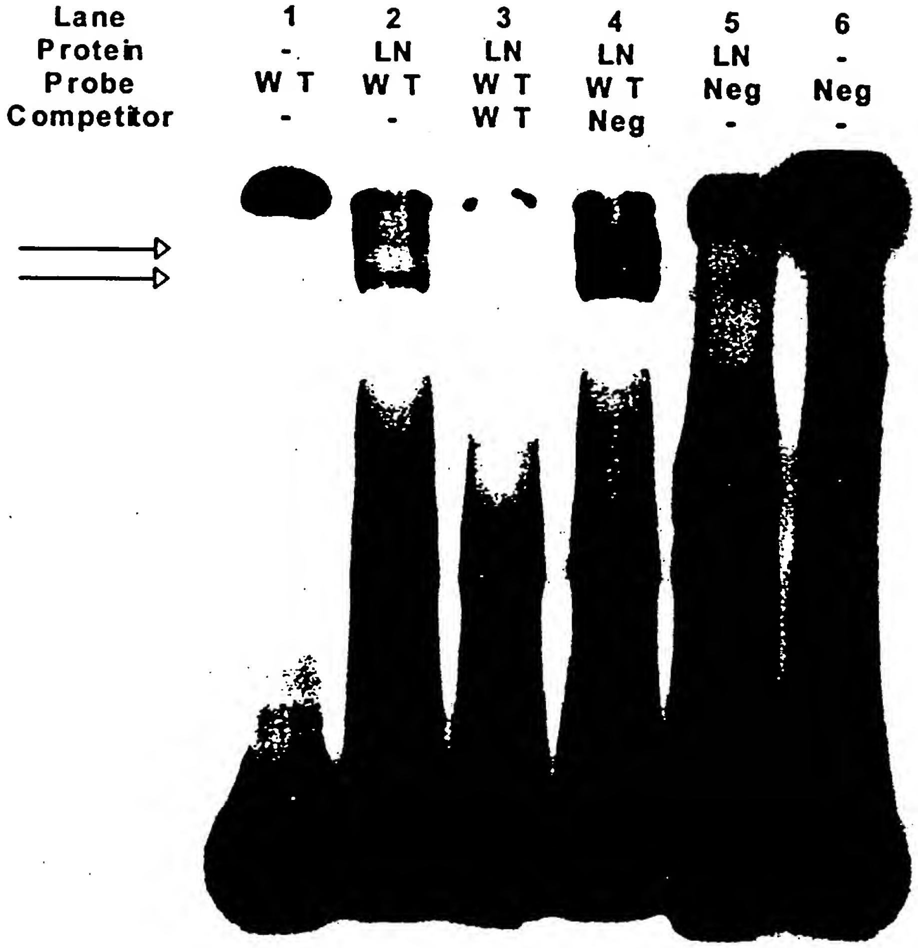

Construct
Luciferase Activity
CN377
CN355
CN378
CN381
CN380
CN379
CN412
CN325
-7020
-2394
-324 +33
-6033
-5155
-4457
-3817
-5155
-3387
-3884
-3387
luc
0 nM
1 nM
0
1000
2000
3000

FIGURE 24B



Lane	1	2	3	4	5	6
Protein	-	LN	LN	LN	LN	-
Probe	W T	W T	W T	W T	Neg	Neg
Competitor	-	-	W T	Neg	-	-

FIGURE 25A

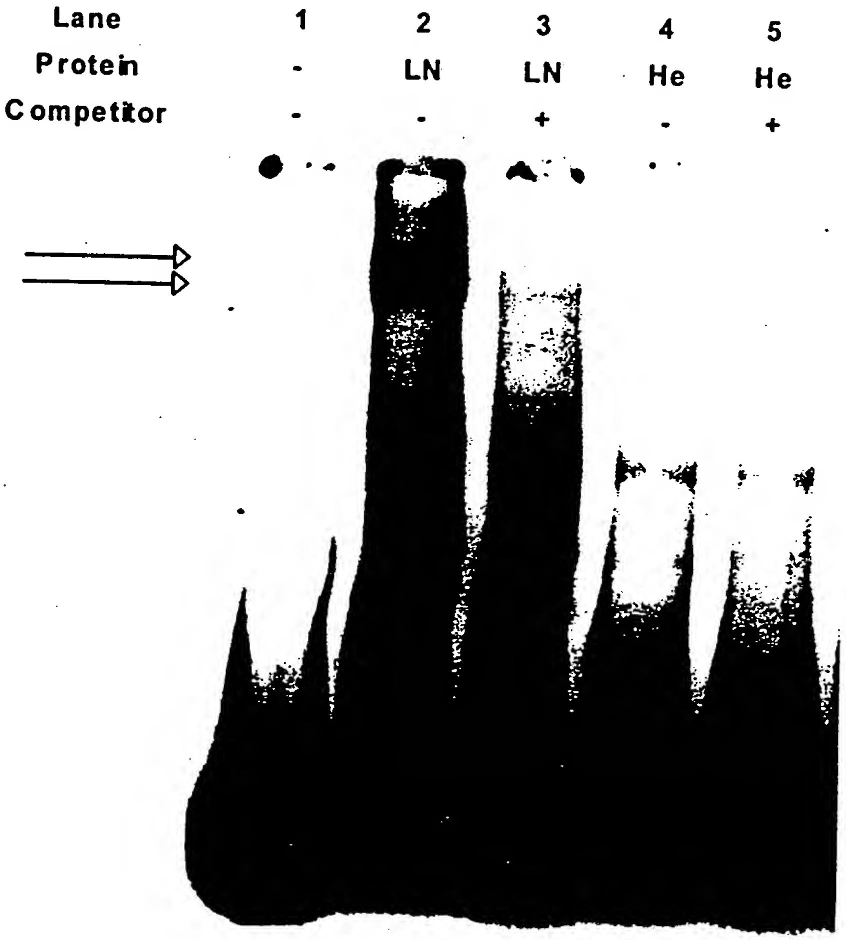


FIGURE 25B

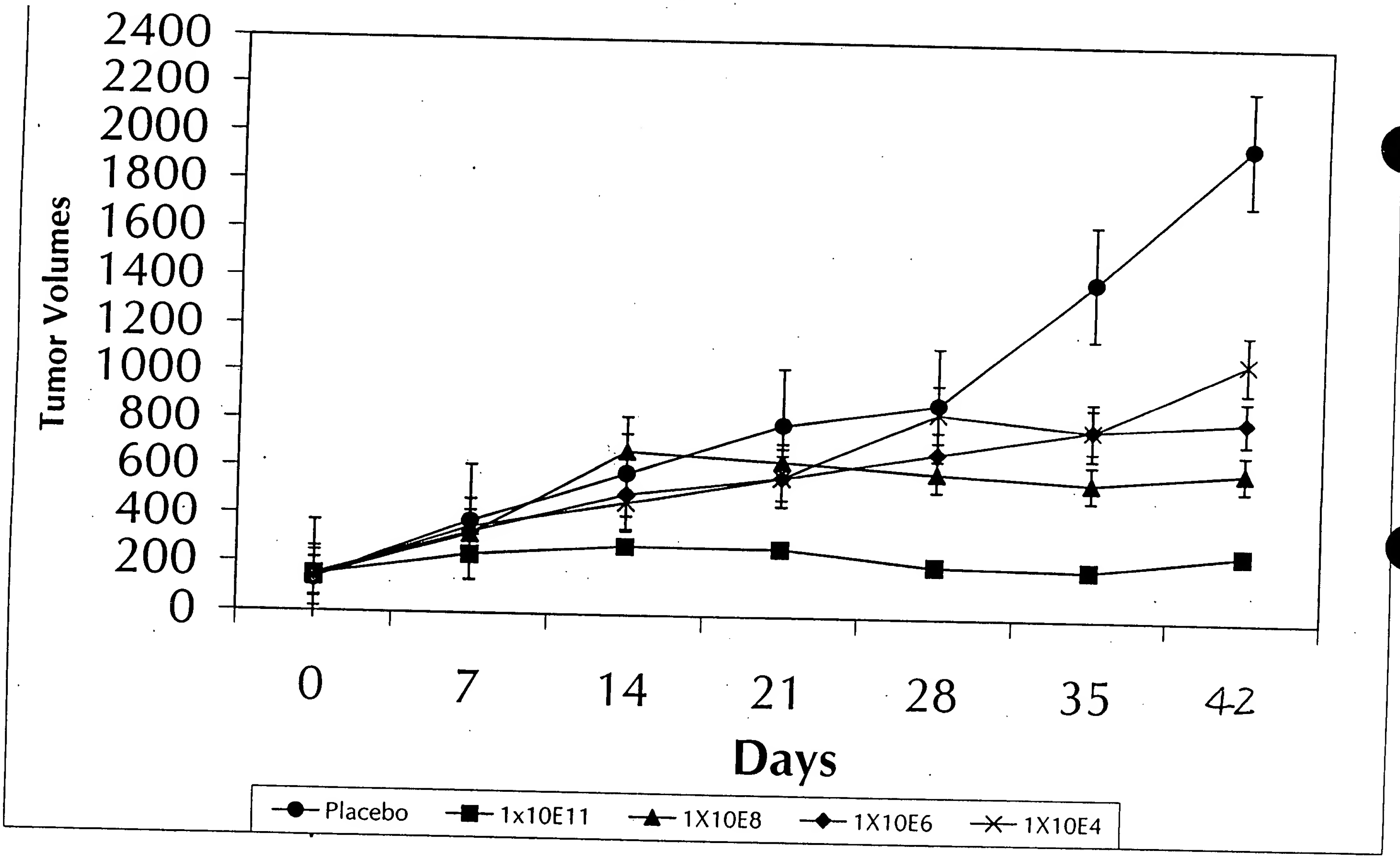

Tumor Volumes
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
0
7
14
21
28
35
42
Days
Placebo
1x10E11
1X10E8
1X10E6
1X10E4

FIGURE 26